

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A., INC.

110 EAST 59TH STREET
NEW YORK, N. Y. 10022
(212) 421-8385

Application for Research Grant

(Use extra pages as needed)

Date: 1974-01-24

1. Principal Investigator (give title and degrees): Tord Kjellström, M.Eng., M.B.

2. Institution & address: Department of Environmental Hygiene
Karolinska Institute
104 01 Stockholm 60

3. Department(s) where research will be done or collaboration provided:

Toyama Prefecture Institute of Hygiene and Medical Microbiology
1-15, Ohtemachi, Toyama City, Toyama Prefecture
Japan

Director: Dr. Kentaro Kubota

4. Short title of study:

Pilot study for setting up a registry of twins reared apart since birth.

5. Proposed starting date: April 1, 1974

6. Estimated time to complete: 1 year

7. Brief description of specific research aims:

Epidemiological studies comparing dizygotic and monozygotic twins discordant within the pairs for some environmental agent (e.g. smoking habits) are powerful for assessing effects or dose-response relationships as the influence of genetic factors can be held under control. However, it has been argued that even in such studies there is still no clearcut division between environment and genetics because twins usually have had very similar environment during childhood when they live together. As twins reared apart from birth are usually very scarce even a small number of such twin pairs could be a useful population for studying concordance rates in behavioural factors (smoking, drinking, stress, personality, type of work, etc.) and clinical indicators (blood pressure, cholesterol in blood, alpha-anti-trypsin, etc.) with pertinence in relation to chronic diseases.

An unique feature of a twin registry in Japan is the possibility of finding twins reared apart from birth. In the past it was not uncommon that twins were separated at birth by one of them being placed in another family.

There may be problems in identifying such twin pairs as efforts were taken to keep the fact of the twin birth secret to the twins themselves. The aim of this pilot study is to investigate how those problems can practically be solved and also, if possible, to set up a registry of twins from Toyama Prefecture and adjacent areas. The goal for this pilot

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7. cont..

registry is 100 complete, living, monozygotic twin pairs reared apart. Other complete twin pairs found as a part of the compilation procedure will be included. If the procedures adopted do not produce any twins reared apart after an initial test period, the project will be stopped and most of the grant will be reimbursed to the Council.

The project will be designed such as to fit into the "International Collaborative Twin Registry".

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2. Brief statement of working hypothesis:

Japanese twins reared apart from birth may be identified through existing administrative records and their present address may be localized.
A limited twin registry consisting of such twins may be set up in Toyama.

3. Details of experimental design and procedures (append extra pages as necessary)

Every family head in Japan has since 1870 a family record, Koseki, where all vital data about the family is included. When a man marries he gets his own Koseki. Births were reported by the family head to the town office and thus included in the Koseki. Every move of an individual registered in the Koseki to another family's Koseki is included.

Since 1945 all births are reported in birth records, Shusseitodoke. From the Shusseitodoke a person can be linked to a Koseki and thus a separation of twins after birth may be identified.

From the Koseki linkage can be accomplished to a registry of the person's present address.

The problem of setting up the twin registry will be attacked from four different directions:

1. Contact will be taken with Japanese scientists making psychosocial studies on twins in order to find twin pairs reared apart from birth, that might be included in this registry.
2. In an epidemiological study on 5,000 women from Toyama in the age groups 45-65 a question about twins in the family is asked by an interviewer. In February, 1974, the answers will be compiled. It can be estimated that an average of 200-300 twin births should exist in this material. Many of them would be the same as those found in procedures 3 and 4 and thus the work of going through family and birth records may be diminished.
3. The family records for men born in Toyama 1880-1900 and 1915-1925 will be gone through until a total of 400 twin births in the first group has been found and 200 in the second group. For each family record the estimated average number of birth is five and the number of twin births per 1,000 births is estimated to six. This means an expected 30 twin births per 1,000 family records. 20,000 such records would have to be gone through to reach the goal above.

The birth records for twins with parents in the 1915-1925 age group will be gone through as a cross-check (twins born after 1945). Apart from this 5,000 randomly selected birth records covering the years 1945-1950 from the same area as the selected family records will be gone through (estimated number of twin birth = 30) in order to get an idea of the prevalence of twin births not being included in the family records.

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The estimated time necessary for looking through one record is two minutes. To go through 25,000 records would take 50,000 minutes, which for two persons means about 400 hours or 12 working weeks when travel time is included.

The procedure above is aimed at finding about 600 twin births in two generations. Approximately half of them will be monozygotic. By linking the data together in this way it will become clear which twin pairs have been reared apart from birth.

The procedures 1 and 2 can be performed at low costs and will be pursued completely. The other procedures will be started on a small scale in order to see if there is reason to believe that twins reared apart can be found at all, and if the goal for this pilot study can be achieved. If the result of this "pilot - pilot" study is negative the project will be stopped and the expenditures will be maximum US\$2,000.

If the result is positive the next step is to find out if the twins found are still alive and to find their present address. The family record of the twins themselves will have to be located and to find addresses the registries used for general elections may be used. This work will for the 600 twin pairs cover approximately another 12 working weeks for two persons. In this pilot study the zygosity of twins found will not be studied and neither will any interviews or clinical tests be done.

If this method for setting up a registry of twins reared apart is successful, in the second year studies of zygosity in combination with questionnaire (by interview) and clinical examination would be performed at a cost of about US\$50 per twin. If 100 monozygotic and 100 dizygotic same-sex pairs are examined the cost would be US\$20,000 + administrative costs. If the resources would be more limited, only zygosity and questionnaire studies would be done at a cost of about US\$20 per twin. The total cost would then be US\$8,000.

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10. Space and facilities available (when elsewhere than item 2 indicates, state location):

Most of the work is clerical and will be done in the offices of the towns selected in Toyama.

For the administration of the project the facilities of the Department of Environmental Hygiene, Karolinska Institute and the Institute of Hygiene and Medical Microbiology in Toyama will be available.

11. Additional facilities required: None

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12. Biographical sketches of investigator(s) and other professional personnel (append): Appendix A + B

13. Publications: (five most recent and pertinent of investigator(s); append list, and provide reprints if available). Appendix C

14. First year budget:

A. Salaries (give names or state "to be recruited")

Professional (give % time of investigator(s)
even if no salary requested)

% time

Amount

Supervisors: Tord Kjellström,
Kentaro Kubota)

5

Research assistant, Sweden
(Ulla Lörich, B.A.)

5

Research assistant, Japan
(to be recruited)

5

REDACTED

REDACTED

Technical

Two clerical assistants, Japan
(to be recruited)

50

REDACTED

Sub-Total for A

REDACTED

B. Consumable supplies (by major categories)

Sub-Total for B

0

C. Other expenses (itemize)

Travel costs Sweden-Japan

4,000

Travel within the investigation area

500

Computer programming and card punching

500

Administrative costs within Japan

1,000

Sub-Total for C

6,000

Running Total of A + B + C

11,000

D. Permanent equipment (itemize)

Sub-Total for D

0

E. Indirect costs (15% of A+B+C)

E

1,650

Total request

12,650

15. Estimated future requirements:

| | Salaries | Consumable Suppl. | Other Expenses | Permanent Equip. | Indirect Costs | Total |
|--------|----------|-------------------|----------------|------------------|----------------|--------------------|
| Year 2 | B | | 25,000 (8,000) | | 4,000 | 31,000 (11,500) |
| Year 3 | | | | | | |

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Other sources of financial support:

List financial support from all sources, including own institution, for this and related research projects.

CURRENTLY ACTIVE

Title of Project

Source
(give grant numbers)

Amount

Inclusive
Dates

PENDING OR PLANNED

Title of Project

Source
(give grant numbers)

Amount

Inclusive
Dates

It is understood that the investigator and institutional officers in applying for a grant have read and accept the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Principal investigator

Typed Name Tord KjellströmSignature *Tord Kjellström* Date 1974-01-23

Telephone

REDACTED
Area Code Number Extension

Responsible officer of institution

Typed Name Margareta AimingTitle Head of AdministrationSignature *Margareta Aiming* Date 1974-01-23

REDACTED
Telephone Area Code Number Extension

Checks payable to

Department of Environmental Hygiene

Mailing address for checks

Karolinska InstituteFack 104 01 Stockholm 60 Sweden

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Appendix A

CURRICULUM VITAE

Tord Kjellström

Born: **REDACTED**

Present employment: research assistant, Department of Environmental Hygiene, Karolinska Institute, Stockholm, Sweden, since 1971.

Mailing address: Department of Environmental Hygiene,
Karolinska Institute
104 01 Stockholm 68"
Sweden
telephone No 08/23 69 00

Education: graduated from Norra Latin High School,

REDACTED

Degree of Bachelor of Medicine from the Karolinska Institute, Stockholm,

REDACTED

Degree of Master of Mechanical Engineering from the Royal Institute of Technology, Stockholm,

REDACTED

Research student at the Department of Mathematical Engineering, Faculty of Engineering, Tokyo University, during 1968.

Passed requirements for Ba in the Japanese language at the Department of Japanese, Stockholm University, March 1969.

Earlier positions: research worker at the National Clinic of Assessment of Work Capacity, during 1966.

Research assistant at the Department of Social Medicine, Faculty of Medicine, Uppsala University, during 1969 and 1970.

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CURRICULUM VITAE

Ulla Lorch

Born: **REDACTED**

Present employment: Research assistant, Department of Environmental Hygiene, Karolinska Institute, Stockholm, Sweden, since May, 1969.

Mailing address: Department of Environmental Hygiene
Karolinska Institute
104 01 Stockholm 60
Sweden
telephone No 08/23 69 00

Education: Graduated from Adolf Fredrik High School,

REDACTED

Degree of Bachelor of Arts from the Stockholm University,

REDACTED

Subjects: major, sociology
minors, statistics and
political science

Publication: Friberg, L., Cederlöf, R., Lorch, U., Lundman, T., DeFairs, U.: Mortality in Twins in Relation to Smoking Habits and Alcohol Problems.

Arch. Environ. Health, 27, 294-304, 1973.

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LIST OF PUBLICATIONS OF TORD KJELLSTRÖM.

1. Kjellström, T.: A Mathematical Model for the Accumulation of Cadmium in Human Kidney Cortex. Nord. Hyg. Tidskr., p 111-119, 1971.
2. Smedby, B., Kjellström, T., and Berfenstam, R.: The Users of Hospital Care (Sjukhusvårdens Konsumenter) Sjukvårdens och Socialvårdens Planerings- och Rationaliseringsinstitut, report No 18, Stockholm, 1972 (in Swedish with summary in English).
3. Kjellström, T., and Friberg, L.: Interpretation of Empirically Documented Body Burdens by Age of Metals with Long Biological Half-Lives with special reference to past changes in exposure. Proceedings, 17th International Congress on Occupational Health, Buenos Aires, September 1972 (in press).
4. Kjellström, T.: An Epidemiological Study on Exposure and Effects of Cadmium. The general and industrial environment of a Swedish lead and copper smelter. (Epidemiologisk expositions- och effektstudie av kadmium. En undersökning av den allmänna och industriella miljön vid Rönnskärsverken). Department of Environmental Hygiene, National Environmental Protection Board, August 1973 (in Swedish).
5. Friberg, L.F., Piscator, M., Nordberg, G.F., and Kjellström, T.: Cadmium in the Environment, 2nd edition, Chemical Rubber Company Press, Cleveland. Ohio (in press).

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